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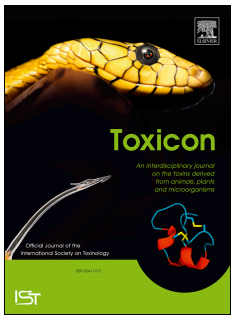

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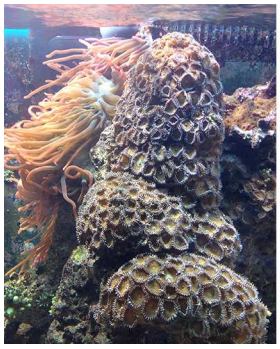

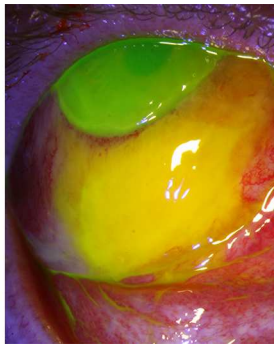

Title

Dangerous reef aquaristics: Palytoxin of a brown encrusting anemone causes toxic corneal reactions

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Abstract

Although frequently observed in domestic saltwater aquariums, literature on exposure to palytoxin (PTX) of encrusting anemones (Zoanthidea) kept in aquariums is rare. Handling these animals for propagation purposes or during cleaning work can lead to dermal, ocular or respiratory contact with the PTX generated by some Zoanthids. The present study describes a case of ocular exposure to liquid from a Zoanthid, which led to corneal ulcers. The patient also suffered from systemic symptoms of dyspnea and shivering and a suspected rhabdomyolysis, which required monitoring in the Intensive Care Unit. After symptomatic treatment provided insufficient results, the corneal ulcers improved with an amniotic membrane transplantation. A review of the literature regarding ocular exposures to this diverse order of Hexacorallia reveals that severe and systemic symptoms can develop with minimal contact.

Keywords

Palytoxin, aquarium, corneal ulcer, amniotic membrane transplantation

1. Introduction

Encrusting anemones (Zoanthidea), also called living stones (Hoffmann, Hermanns-Clausen et al. 2008), are colony-forming soft corals. These Cnidarians are commonly found in coral reefs, in the deep sea and in many other marine environments around the world. Encrusting anemones vary in size and color, ranging from mud brown to fluorescent green and purple. Because they can be easily grown, encrusting anemones are widely spread among domestic reef aquariums (Deeds, Handy et al. 2011). Less widely known is the fact that some species produce palytoxin (PTX) as a defense mechanism (Deeds and Schwartz 2010). PTX is an extremely potent toxin used by various marine organisms (Gleibs and Mebs 1999) including many Zoanthids, such as the *Palythoa* species (Ramos and Vasconcelos 2010). The toxin destroys the ionic gradient of the cells by changing their membrane Na/K–ATPase pumps into non-selective cationic pores (Hoffmann, Hermanns-Clausen et al. 2008; Wu 2009). PTX is very potent; hence, minimal amounts are sufficient to cause medically relevant intoxication or damage. Several reports describe oral, dermal and inhalational intoxication after suspected PTX exposure, sometimes with systemic symptoms (Habermann 1989; Artigas and Gadsby 2003; Wieringa, Bertholee et al. 2014; Cortini 2015). To our knowledge, only one report with two cases has been published regarding accidental ocular PTX contact in humans (Moshirfar, Khalifa et al. 2010).

We present the case of a severe toxic corneal reaction caused by an accidental splash of an encrusting anemone's fluid into the eye while the subject was handling this Zoanthid out of water. The patient suffered severe systemic symptoms. This case shows that ocular PTX contact can cause austere toxic reactions that include corneal ulcers and systemic symptoms. In our case, amniotic membrane transplantation presented a good therapeutic option.

2. Case report

An otherwise healthy 63–year-old man presented to the Emergency Unit and reported that an encrusting anemone had squirted into his right eye while he was cleaning his aquarium (**Fig. 1** and **2**). Immediately after contact, he felt a burning sensation in his right eye and rinsed it with tap water for several minutes. He subsequently tried to treat the symptoms with chamomile and black tea. Two and a half hours after the incident, dyspnea, nausea and shivering developed, causing him to go to the hospital. Upon admission, the patient's blood pressure was 135/73 mm Hg and his heart rate was 102 beats per minute. The electrocardiogram showed no arrhythmia. Oxygen saturation was 94%. The serum white blood cell count (20.29 $x10^9$/L; reference range 3.5–10.0 $x10^9$/L) and C–reactive protein (47.4 mg/L; <10.0 mg/L) were elevated. Thrombocytes (312 $x10^9$/L; 150–450 $x10^9$/L), erythrocytes (5.32 $x10^9$/L; 4.50–6.30 $x10^9$/L) and serum electrolytes such as sodium (139 mmol/L), potassium (3.7 mmol/L) and calcium (2.15 mmol/L)

were in the normal range. The patient had a slightly elevated creatine kinase (261 U/L; 50-200 U/L) and lactate dehydrogenase (267 U/L; 135–225 U/L) and a positive urine examination for myoglobin (39 µg/l; <21 µmol/L); suggestive of possible rhabdomyolysis. This required monitoring the patient in the intensive care unit. The prophylactic treatment consisted of intravenous infusion of balanced crystalloid solutions (Plasma-Lyte®, Baxter AG, Volketswil, Switzerland). On the second day, all tested laboratory parameters were better and the patient was discharged from the hospital.

Initially, both eyes showed a strong conjunctival injection and superficial corneal punctate epitheliopathy. The right eye was more affected, exhibiting multiple corneal Descemet's folds. The pH was elevated to 8.5 on the right eye and 7.5 on the left. After rinsing with Diphoterine® (aqueous solution containing amphoteric salts), the pH of the right eye was lowered to 7.5 and the pH of the left eye was lowered to 7.0. The subject's visual acuity in both eyes was reduced to counting fingers. The intraocular pressure and fundus examination were unremarkable. An empirical therapy with antibiotic and steroid drops was initiated immediately.

On the second day, both eyes exhibited incomplete corneal erosion and anterior chamber reactions, the right side being more severely affected. In addition, both eyes showed Descemet's folds, and the conjunctiva was partially avascular (**Fig. 3**). Visual acuity had improved to 0.2 on both sides. Regular controls in the eye clinic showed no further improvement. Despite treatment with a topical steroid and antibiotics, the corneal erosions did not heal, and ulcers developed one week after the accident. Finally, amniotic membrane transplantations were performed on both eyes (**Fig. 4**). Within several weeks the cornea healed, with residual thinning. Four months after the exposure, scleral contact lenses were fitted to correct the remaining irregular corneal astigmatism. With scleral contact lenses, visual acuity recovered to 0.8 in the right eye and 1.0 in the left eye (**Fig. 5**).

3. Review of the literature

An extensive literature search revealed only one publication regarding ocular contact with Zoanthids (Moshirfar, Khalifa et al. 2010). However, according to on-line marine aquarium forums, ocular contact is more common than it appears (3reef ; Cap-refical ; Manhattenreefs ; Meerwasser-Lexikon ; Meerwasserforum-Bayer ; Meerwasserriff-Forum ; Meerwasserverein ; Nano-reef ; Recifalouest ; Reefcentral ; Reefsmagazine). Including these blogs, 15 ocular exposures (of which 14 concerned men) have been recorded. The subject's age was known in only three cases (31 and 49, (Hoffmann, Hermanns-Clausen et al. 2008) and 63, our patient). Most accidents happened while fractioning or otherwise handling Zoanthids outside the water. Eight patients described the feeling of "being squirted in the eye"; in three cases, they rubbed their eyes after dermal contact without previously washing their hands, while no exposure

mechanism was given in four cases. Except for two patients, all patients immediately rinsed their eyes, yet all reported intense pain, redness, and swelling. In seven cases, the redness and swelling progressed to corneal inflammation and ulceration with partial loss of vision. In three cases, systemic symptoms of nausea, fever and shivering were mentioned. Only seven cases provided a detailed description of the clinical course, duration of symptoms and treatment. In these cases, the symptoms lasted between four days and seven months, with most symptoms resolving within four to five weeks.

A variety of measures were taken to treat accompanying symptoms with varying success, including rinsing the eyes with water and administering artificial tears, ocular and oral steroids, antibiotics and pain relief. One patient received contact lenses four years after the accident to help with diminished vision. Unfortunately, there were no further specifications.

Exact identification of the Zoanthids involved in the aforementioned cases was not possible, as the Latin or even common name was often unknown to the owners or was simply not mentioned. Only very few of the involved specimens were mentioned (1x *Zoanthus gigantus*, 1x Purple death – a common name for *Palythoa singaporensis*, 1x *Protopalythoa sp.*, and 1x *Zoanthus sp.* (Reefsmagazine ; Reimer 2009)). Nonetheless, all the aforementioned reports were posted under Zoanthid threads. The fact that only few species of two genera have been proven to possess PTX (*Palythoa caribeaorum, mammilosa, tuberculosa, toxica, vestitus* and *aff. margaritae* and *Zoanthus solanderi* and *sociatus)* does not preclude others from doing so *(Wu 2009)*. In addition to Zoanthids, other marine organisms can produce PTX (i.e., *Ostreopsis sp., Lophozosimus pictor*, and others (Wu 2009; Cortini 2015)). A large number of incidents involving aerosol contact with PTX occurred during the *Ostreopsis ovata* algae bloom in northern Italy in 2005 (Tubaro, Durando et al. 2011), in which 209 symptomatic cases were recorded (33 of which complained of lacrimation) (Durando, Ansaldi et al. 2007), and in 2006, in which there were 19 symptomatic cases (one patient with lacrimation) (Durando, Ansaldi et al. 2007).

4. Discussion

Aquariums can be found in many households, and seawater or reef aquariums are becoming increasingly popular. With some of the toxin-producing species that can be found in a seawater aquariums, it is astonishing there have not been more cases of medically relevant contact. The literature shows a variety of cases in which owners were exposed to PTX generated by soft corals (Hoffmann, Hermanns-Clausen et al. 2008; Reimer 2009; Wu 2009; Deeds and Schwartz 2010; Moshirfar, Khalifa et al. 2010; Nordt, Wu et al. 2011; Tubaro, Durando et al. 2011; Bernasconi, Berger et al. 2012; Wieringa, Bertholee et al. 2014; Cortini 2015). PTX destroys the ionic gradient of cells by changing their membrane Na/K–ATPase pumps into non-selective cationic pores (Habermann 1989; Artigas and Gadsby 2003; Moshirfar, Khalifa et al. 2010). The

exact in vivo toxicity mechanism is not fully understood (Wieringa, Bertholee et al. 2014; Berni, Bellocci et al. 2015). Initial mammal studies (Wiles, Vick et al. 1974; Cortini 2015) showed a high mortality rate due to PTX ingestion and injection as well as a wide range of morbidity due to ocular, dermal and inhalational exposure. In these experiments, irreversible ocular damage was induced at a dose of 0.4 μg/kg. The damage observed was mainly due to corneal scars and synechiae.

The mechanism of PTX production remains unclear. One possible origin involves the *Ostreopsis* dinoflagellates that live in the water column or sand around *Palythoa spp.* Another source may be bacteria. However, this does not explain how colonies in captivity (as in aquariums) can contain PTX long after having been removed from their natural habitats. For example, poison dart frogs cease to be toxic if bred in captivity. One explanation may be that PTX poisoning is caused by a bacterium in the gut of the Palythoa (personal communication to JF by James Reimer). Although it is known that Zoanthids exude a profuse slime when disturbed (Habermann 1989; Deeds, Handy et al. 2011), Zoanthid squirting, though not previously been described in the scientific literature, is thought to be the result of applying pressure on the specimen while fractioning it for propagation purposes (personal communication to JF by James Reimer) or as a result of rapid closing, which can unintentionally release a tiny stream of water (Artigas and Gadsby 2003; Rossini 2014).

Because Zoanthids belong to the subclass Hexacorallia, they sting as well as produce toxins, which may explain some of the symptoms, as discussed by Glasser, Noell et al. (Glasser, Noell et al. 1992), Steel (Steel 1993) and Keamy, Umlas et al. (Keamy, Umlas et al. 2000) where ocular exposure with corals and jellyfish resulted in transient keratitis, keratoconjunctivitis and blurred vision.

Two of the three patients who rubbed their eyes progressed to severe symptoms, including corneal ulcers that lasted for many weeks. This seems to indicate that rubbing produces stronger symptoms, i.e., more intense contact with PTX, even though case numbers are too small to allow for a determination of statistical relevance. The fact that our patient was squirted only in the right eye but developed symptoms in both eyes may be explained by the possibility that irrigating the right eye brings the left eye (and skin) in contact with the toxin as well.

Several limitations must be taken into consideration with regard to the available literature and the reports in different blogs of the Seawater Aquarium Society. Interpretation of blog reports is difficult because there has been considerable retelling of the same cases in different blogs by different people, much of which must be considered hearsay. We tried to exclude all obvious double or triple entries. Furthermore, exact classification of the Zoanthids involved is difficult, and the exact species are often unknown, even to their owners. In addition, an underreporting

bias likely exists. A further and unfortunate 1limitation in our case was that we only had a photo provided by the patient to determine the causative genus of the Zoanthid involved because the patient disposed of his specimen directly after his painful encounter. Hence, accurate identification of the exact species was not possible, and the PTX content could not be measured.

5. Conclusions

The risk of PTX exposure from home marine aquariums is a largely underestimated threat to safety (Wiles, Vick et al. 1974; Hoffmann, Hermanns-Clausen et al. 2008; Deeds, Handy et al. 2011). Wiles, Vick et al. stated that a dose of 0.4 µg/kg was enough to lead to irreversible visual impairment due to corneal scars and synechiae, and that rinsing of the eye could not completely abrogate the toxic effects (Wiles, Vick et al. 1974). Nonetheless, rapid and thorough irrigation of the affected eye is important. Care should be taken to rinse both eyes independently, as the strong toxin may cause a toxic reaction even in the previously unaffected eye. Empirical therapy includes artificial tears, topical steroids and antibiotic drops. In the case of keratolysis and ulcer development, amniotic membrane transplantation may be a good therapeutic option. Reef aquarium enthusiasts should always wear protective gloves and goggles while handling Zoanthids to protect against possible PTX secretion and to prevent ocular, dermal and systemic intoxications (Deeds, Handy et al. 2011; Nordt, Wu et al. 2011; Rossini 2014).

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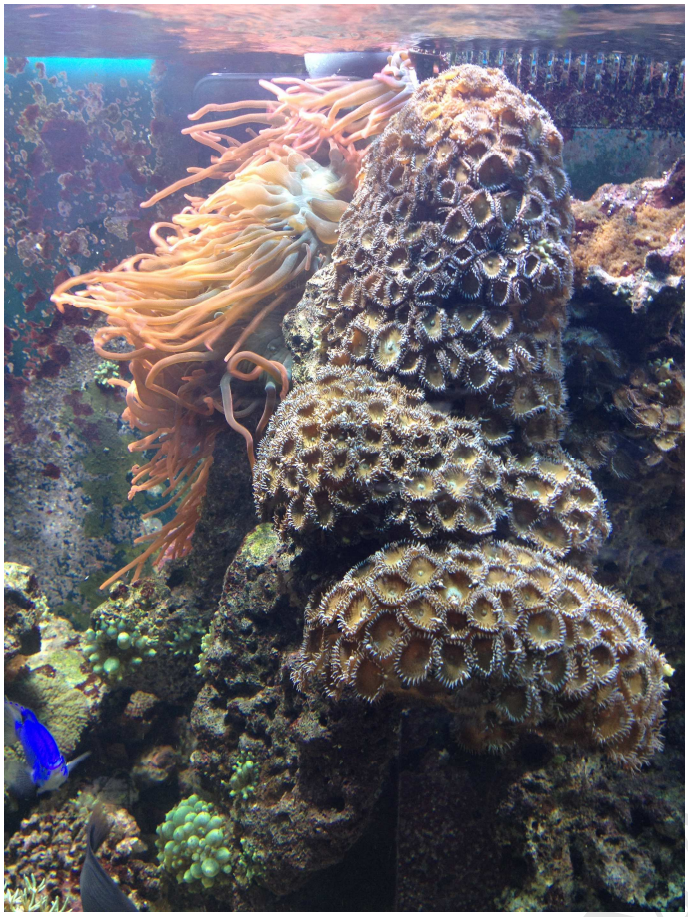

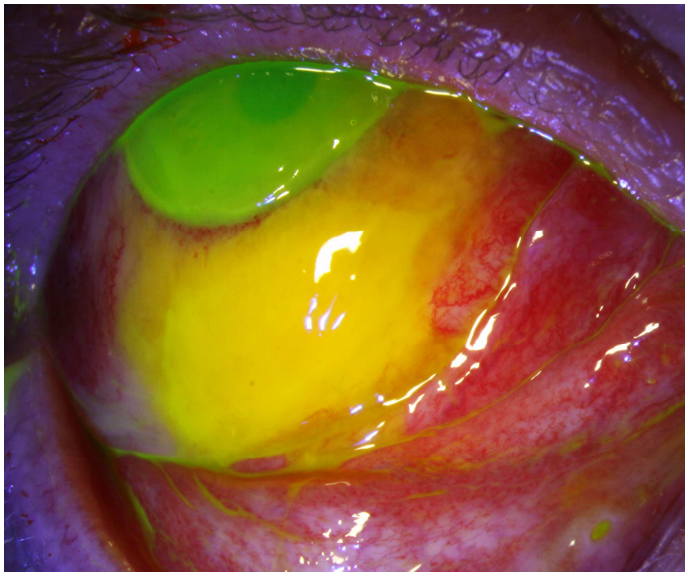

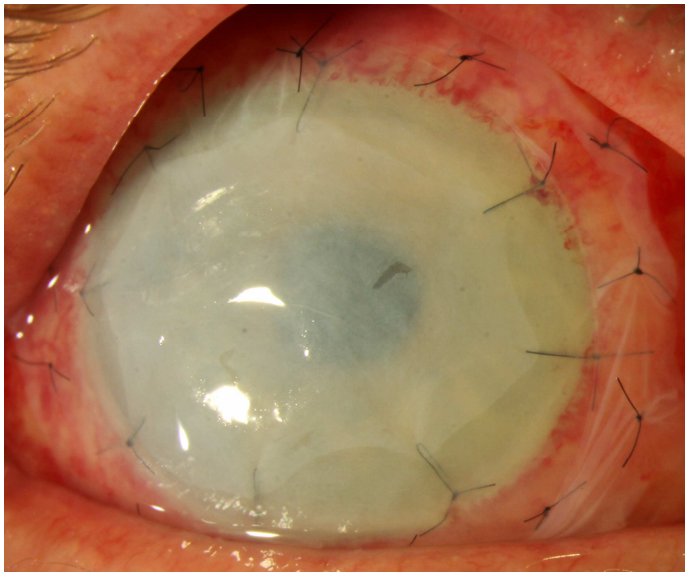

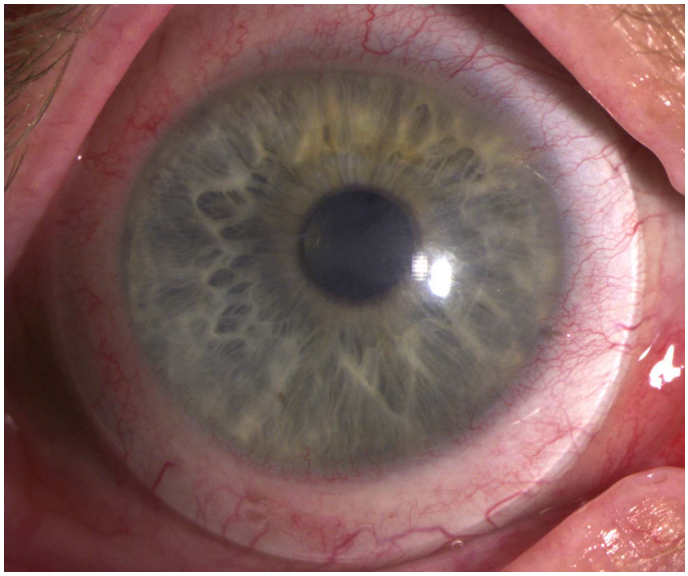

- Literature on exposure to palytoxin of anemones kept in aquariums is rare.
- Ocular contact with an anemone's fluid caused a toxic local and systemic reaction.
- Severe corneal ulcers developed.
- Corneal ulcers were successfully treated with amniotic membrane transplantation.